have MRI abnormalities such as cartilage damage, bone marrow lesions, or meniscal extrusion. Those with the medial regional pain were also more likely to have meniscal damage (Table 1).

Table 1

| Compartment-specific MRI features* | Local Medial Joint Line Pain (n = 83) | | | Regional Medial Pain (n = 36) | | | Global Pain (n = 27) | | |
|---|---|---|---|---|---|---|---|---|---|
| | RRR | [95%CI] | | RRR | [95% CI] | | RRR | [95% CI] | |
| Cartilage damage | 2.52 | 1.07 | 5.92 | 3.97 | 1.28 | 12.35 | 4.65 | 1.37 | 15.81 |
| Bone marrow lesions | 9.89 | 2.04 | 47.99 | 12.10 | 2.27 | 64.60 | 12.44 | 2.24 | 69.05 |
| Synovitis/effusion** | 0.99 | 0.46 | 2.14 | 1.62 | 0.61 | 4.28 | 0.94 | 0.31 | 2.79 |
| Meniscal damage | 1.46 | 0.56 | 3.77 | 3.72 | 1.10 | 12.60 | 2.65 | 0.77 | 9.11 |
| Meniscal extrusion | 1.08 | 0.47 | 2.49 | 8.77 | 2.18 | 35.23 | 3.46 | 1.00 | 12.05 |

*adjusted for age, sex and BMI and compared to knees with pain in the past 30 days; RRR = relative risk ratio, CI = confidence interval. ** Synovitis/effusion was read for the whole knee.

Based on the results from the table above, MRI features from the medial compartment were then combined into a single multivariable, multinomial model predicting each of the three patterns of knee pain. In this single multivariate multinomial model taking into account all the MRI features, bone marrow lesions were still significantly associated with local medial joint line pain, medial regional pain and global pain when compared to no pain. RRRs and 95% CIs were 7.97 (1.48, 43.01), 8.56 (1.45, 50.4), and 8.04 (1.35, 48.0), respectively. Meniscal extrusion was significantly associated with medial regional pain, with an RRR of 6.76 (1.574, 29.05) after accounting for the other MRI abnormalities.

**Conclusions:** The presence of MRI-detected pathology was associated with medial localized joint line pain, medial regional pain and global pain patterns. Of note, meniscal extrusion was associated with the medial regional knee pain pattern. The association of meniscal damage with the medial regional knee pain pattern was no longer significant after accounting for meniscal extrusion. These findings may help to identify more homogenous populations for targeted knee OA interventions.

## 13
## OSTEOARTHRITIS SEVERITY IS ASSOCIATED WITH INCREASED RISK FOR DIABETES AND HEART DISEASE

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**Purpose:** Prior studies have documented increased rates of diabetes and heart disease in individuals with versus without osteoarthritis (OA). However, there is a paucity of research that has examined if OA severity contributes independently to these relationships. Our study aim was to evaluate the relationship between OA severity and prevalence of heart disease and diabetes and the extent to which these relationships, if found, were explained by common risk factors.

**Methods:** In a population cohort with hip and knee OA, standardized interviews assessed sociodemographics, OA severity (WOMAC subscale and summary scores), body mass index (BMI, from height and weight), general health status (SF36) and comorbidity (list of 13 non-musculoskeletal, MSK, conditions). Diabetes and heart disease were defined as present if the participant reported having 'ever' received a diagnosis or received treatment in the past year. Logistic regression was used to examine the association of OA severity with each of diabetes and heart disease, first unadjusted, then controlling for potential confounders (age, sex, education, income, BMI and diabetes [heart disease model]). We assessed for potential interactions between OA severity and age, sex, education, and income, and between OA severity and diabetes on heart disease. Statistical significance was considered at a 2-tailed level of 0.05.

**Results:** Participation rates were 80.6% and 75.4% for the rural and urban regions, respectively. Analyses are based on 2,225 participants with OA. Their mean age was 70.7 years, 72.0% were female and 96.1% Caucasian; 81.1% reported ≤ high school education and 63.9% reported an annual income ≤ $20,000. WOMAC scores indicated moderate to severe OA pain and disability. Participants' mean BMI was 27.9 kg/m$^2$; 38.8% were overweight and 30.9% were obese. Three-quarters (73.1%) reported receiving treatment for at least one other non-MSK chronic condition; one-fifth (22.5%) reported 3 or more comorbid conditions; 30.4% reported heart disease and 16.8% reported diabetes. Unadjusted for other factors, a 10-point increase in WOMAC summary scores was associated with a 10% increase in the odds of self-reporting diabetes (odds ratio 1.10; 95% confidence interval 1.04–1.16). This relationship was attenuated, becoming non-significant, after controlling for BMI. Unadjusted for other factors, a 10-point increase in WOMAC summary scores was associated with a 12% increase in the odds of reporting heart disease (odds ratio 1.12; 95% confidence interval 1.06–1.17). In adjusted analyses, self-reported heart disease was significantly and independently associated with male sex, lower income, and interactions between OA severity and each of age (p value for the interaction = 0.015) and self-reported diabetes (p value for the interaction = 0.02); the effect of a 10-point increase in WOMAC summary scores on the odds of self-reporting heart disease decreased with increasing age, but was significantly greater at all ages among those with than among those without comorbid diabetes. Results were similar using the WOMAC pain or function subscale scores to define OA severity (data not shown).

**Conclusions:** In a population cohort with moderately severe hip and knee OA, the prevalence of comorbid diabetes and heart disease was substantial and positively linked to increasing symptomatic OA severity. For diabetes, this relationship was explained by a common risk factor, obesity. For heart disease, this relationship remained significant even after controlling for common risk factors, and was stronger among those with versus without comorbid DM. Prospective studies are needed to further elucidate the causal relationships among these common conditions.

## 14
## SERUM ADIPOKINES IN END-STAGE OSTEOARTHRITIS; COMPARISON WITH HEALTHY CONTROLS AND RELATIONS WITH INTRA-ARTICULAR JOINT CHARACTERISTICS

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**Purpose:** Obesity is an important risk factor for osteoarthritis (OA). The body mass index (BMI) is strongly associated with the prevalence and incidence of knee OA. It is established that metabolic factors exert an extra systemic effect on top of the mechanical effect of overweight in OA. Adipose tissue is considered an endocrine tissue that releases cytokines, such as IL-1 and TNFα, as well as adipokines, such as adiponectin, leptin, and resistin. Adipokines have been reported to be involved in the disease process. The exact mechanisms by which adipokines exert their effects in OA are still unclear. The aim of this study is to compare serum adipokines in end-stage OA with healthy controls and to evaluate the relationship of these serum adipokines with actual cartilage damage and synovial inflammation in the affected joint.

**Methods:** 172 successive patients with severe knee OA selected for total knee replacement (TKR) surgery were included at the Sint Franciscus Gasthuis, Rotterdam. Serum was collected shortly before TKR surgery. Additionally from a healthy control (HC) group of 132 individuals without any sign of radiographic knee OA serum was collected as well. Of all end-stage OA patients and healthy individuals characteristics were collected and serum adipokine (adiponectin, leptin and resistin) levels measured by ELISA. Of the OA patients cartilage and synovial tissue were collected at joint replacement surgery. Histological damage and proteoglycan turnover and histological inflammation and IL-1β and TNFα production were measured of cartilage and synovium, respectively. The study was conducted according to the declaration of Helsinki and received ethics approval of the hospital.

**Results:** In OA patients adiponectin levels were inversely related with BMI (R = −0.218, p = 0.004) and positively correlated with age (R = 0.283, p = 0.000). Levels were higher in women than in men (24±13 and 14±7 μg/ml, p = 0.000). Leptin levels showed a positive correlation with patients BMI (R = 0.604, p = 0.004 and R = 0.495, p = 0.000, for OA and HC, respectively). Leptin levels were also higher in women than in men (90±64 and 33±28 ng/ml, p = 0.000 in OA; 22±11 and 5.3±3 ng/ml, p = 0.000 in HC). In OA, resistin levels were inversely related with age (R = −0.206, p = 0.012). Resistin levels did not differ between women and men.

For the OA patients, all three adipokines correlated positively with synovial inflammation. For adiponectin, leptin and resistin with synovial tissue IL-1β production (p = 0.02 all (p = 0.04 for women), p = 0.09 all, and p = 0.02 men, respectively). For leptin and resistin with synovial tissue histological inflammation (p = 0.06 all (p = 0.02 in men) and p = 0.09 all, respectively). For resistin with TNFa (p = 0.09 all, p = 0.02 for men). None of the adipokines showed an association with histological or biochemical cartilage characteristics.